PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA2004/000073	21.01.2004	21.01.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/24, A61K45/06

Applicant
SMARTRIX TECHNOLOGIES INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2004/000073

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 28, 29

because:

☒ the said international application, or the said claims Nos. 28, 29 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-64
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-64
Industrial applicability (IA)	Yes:	Claims	1-27, 30-64
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 28 and 29 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:
D1: WO 02/098352 A
D2: WO 02/066002 A

Novelty

1 - Present claims 1-64 are considered to be novel (Article 33(2) PCT).

Inventive step

2 - The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-64 does not involve an inventive step in the sense of Article 33(3) PCT.

3 - The document D1 is regarded as being the closest prior art. It discloses (page 3, line 30 - page 6, line 13; examples; claims) a composition comprising an acid inhibitor, preferably an H2 blocker such as famotidine, and an NSAID. The composition is particularly useful for patients with osteoarthritis. In example 4, such a composition is disclosed comprising a controlled release core comprising naproxen, famotidine and hydroxypropylmethylcellulose, an enteric coating around said core, and an outer coating comprising famotidine to provide rapid release.

The subject-matter of independent claims 1 and 2 (which only differ by an optional feature) therefore differs from this known composition in that the first drug composition and the sustained release second drug composition are separated in two layers (in example 4 of D1 both are combined in one homogeneous core), and in that the immediate release composition of the second drug is in contact with the composition of the first drug (in example 4 of D1 an enteric coat separates core and immediate release coat).

The application does provides any technical effect for the above differences.

Hence, the problem to be solved by the present invention can only be seen as to provide an alternative dosage form comprising an extended release NSAID and an H2-receptor antagonist.
The solution proposed in claims 1 and 2 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT).
With regard to the core comprising two different drugs: providing such a core in layered form, with each drug separated in a distinct layer, is an obvious alternative to mixing two drugs in one core. Regarding the coating: D1 also foresees bi-layer tablets, without a coating separating the core and the outer coating (page 11, lines 16-21; claim 14).
Thus, in the absence of any unexpected effects, no inventive step can be recognised in the subject-matter of claims 1 and 2.
4 - The same reasoning applies, mutatis mutandis, to the subject-matter of the corresponding independent claims 28-30, 55 and 60, which therefore are also considered not inventive.
5 - Additionally, with regard to inventive step of claims 1 and 2, it has to be noted that in general a technical problem can only be taken into account in the assessment of inventive step if it can be accepted as having been successfully solved. When only some and not substantially all of the claimed subject-matter exhibits a particular technical effect, the conclusion must be that the invention as broadly defined in the independent claims is not a solution to the technical problem of achieving the technical effect, with the consequence that the alleged technical effect of some of the claimed subject-matter is to be disregarded when determining the objective problem underlying the invention and thus when assessing inventive step.
At present notably claims 1 and 2 are so broadly formulated that it is highly unlikely that all compositions falling under these claims solve the problem of providing an (improved) oral dosage form comprising an extended release NSAID and an H2-receptor antagonist for the treatment of osteoarthritis in patients at an elevated risk for developing gastrointestinal side effects (see page 4, lines 23-26).
Therefore, notwithstanding the objection under point 3, present claims 1 and 2 are in any case considered to lack an inventive step.
6 - Dependent claims 3-27, 31-54, 56-59 and 61-64 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, see documents D1 and D2 and the corresponding passages cited in the search report.

Industrial applicability

7 - Claims 1-27 and 30-64 comply with Article 33(4) PCT (see also Item III).